

REMARKS

With entry of this amendment, claims 45-48 are pending in the application. By this amendment, claims 25 and 30 have been cancelled, without prejudice. Claims 1-24, 26-29, 31-44 and 49-56 were previously canceled without prejudice. Applicants continue to reserve the right to pursue the subject matter of all canceled claims in one or more related applications. All of the amendments herein are fully supported by the disclosure, and no new matter has been added to the application.

Patentability Under 35 USC § 112

Claims 45 and 48 are rejected under 35 USC § 112, second paragraph for alleged failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention (Office Action at p. 2). In particular, the Examiner indicates that claim 45 is a duplicate of claim 25 and claim 48 is a duplicate of claim 30.

Claims 25 and 30 have been cancelled, thereby removing the grounds for this rejection. Therefore, the rejection should be withdrawn.

Patentability Under 35 USC § 103

Claims 25, 30, and 45-48 are rejected under 35 USC § 103(a) as allegedly unpatentable over Beer et al., US 6,204,284 B1, for reasons as set forth in the prior Office Action dated September 21, 2004.

Applicants respectfully traverse the foregoing grounds of rejection and submit that the subject matter of claims 25, 30 and 45-48 is neither disclosed nor suggested by Beer et al., US 6,204,284 B1—based on the facts and reasoning set forth herein below, and as presented in the Amendment dated February 22, 2005 (“Prior Amendment”), and in view of the entire record in this application.

In maintaining the instant rejection, the Office continues to minimize the differences between the racemic mixture of Beer et al. and the compounds of the present invention which are substantially free of the (+) enantiomer. Although the Office continues to assert that the (-) isomer of the present invention and the racemate of Beer et al. “have both isomers except in degrees,” there is no evidence provided by the Office regarding how much of each isomer is contained in the racemic mixture of Beer et al. On the other hand, the instant specification clearly teaches that “[t]he term “substantially free of its corresponding (+) enantiomer means containing no more than about 5% w/w of the corresponding (+) enantiomer.” (Specification, p.6, paragraph [0029]). It is also clear from the specification that the (-) isomer of the present

invention has substantially and unexpectedly different biological properties as compared to the racemic mixture of Beer et al.. In particular, the data in Table 1 on page 23 of the specification shows that while both the racemic mixture and the isolated (-) isomer have affinity for the dopamine reuptake site of the dopamine transporter, the racemic mixture actually has a *higher* binding affinity for this site than the (-) isomer. That is, the (-) isomer is not *more* reactive, but is in fact *less* reactive, than the racemic mixture. Furthermore, the data in Tables 2 and 3 on page 23 of the specification indicate that the racemic mixture has affinity for the norepinephrine uptake site of the norepinephrine transporter and the serotonin uptake site of the serotonin transporter, while the (-) isomer exhibited no measurable affinity for these sites.

It should be noted that Beer et al. repeatedly asserts that inhibition of the uptake of 5-hydroxytryptamine, norepinephrine *AND* dopamine is needed for effective treatment of addictive disorders. For example:

It has also been found that 1-substituted--(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexanes can inhibit the uptake of 5-hydroxytryptamine (5-HT), norepinephrine (NE) and dopamine (DA) in crude rat brain synaptosomal preparations, and may be useful, therefore, as agents for the treatment and relief of addictive disorders such as chemical substance abuse, eating disorders resulting in anorexia or obesity and other compulsive disorders. [Beer et al., column 2, lines 18-26]

It is also asserted in Beer et al. that 1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane is a selective 5-HT reuptake inhibitor. In particular:

The results of this experiment show that 1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane, *a selective 5-HT inhibitor*, does provide an attenuation in ethanol consumption in rats. [Beer et al., column 5, lines 49-52, emphasis added]

There is no indication or suggestion in Beer et al. that an isolated (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane, which Applicants have shown to have no measurable affinity for the norepinephrine uptake site of the norepinephrine transporter and the serotonin uptake site of the serotonin transporter, can be effectively employed as in Applicants' invention to prevent or treat addictive disorders.

The Office has previously acknowledged the novelty and nonobviousness of Applicants' compositions comprising a resolved (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane. In particular, Applicants' issued US Patent No. 6,569,887 B2,

which claims (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane and compositions containing (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane, was considered and issued by the Office over US Patent No. 4,118,417 disclosing the racemic mixture of the compound. The Office similarly considered and issued US Patent No. 6,716,868 B2 to Applicants claiming methods of treating or preventing disorders alleviated by inhibiting dopamine reuptake using (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane.

In view of the foregoing, Applicants respectfully submit that the Office has not established *prima facie* evidence that the instant claims are unpatentable over Beer et al., or, alternatively, that the instant disclosure, evincing usefulness of the (-) isomer within the presently-claimed methods, fail to establish "unexpected results" sufficient to overcome such *prima facie* evidence, if found. Applicants respectfully submit that the facts of record clearly establish novelty and nonobviousness of the pending claims directed to the prevention or treatment of specific disorders alleviated by inhibiting dopamine reuptake using (-)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane, whereby the pending rejection of claims 25, 30, and 45-48 under 35 USC § 103(a) over Beer et al., US 6,204,284 B1 is believed to be overcome.

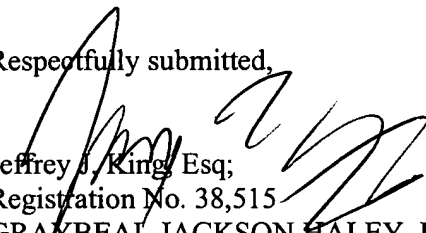
CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at (425) 455-5575.

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Respectfully submitted,


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